93%), 182 (M^+· – $CH_3NHCONCH_3$, 100%).

Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.59; H, 5.81; N, 15.36.

3,4-Dihydro-1,3-dimethyl-4-(2-hydroxyphenyl)pyrido[2,3-*d*]pyrimidin-2(1*H*)-one (8a). To a solution of 9.0 mL (0.064 mol) of freshly distilled diisopropylamine in 150 mL of dry THF held at –40 °C under a N_2 atmosphere was added 26.5 mL of 2.4 M *n*-butyllithium/hexane (0.064 mol). After being stirred at –20 °C for 0.5 h, the LDA solution was cooled to –40 °C and a solution of 16.0 g (0.059 mol) of **4** in 50 mL of dry THF was added over 0.25 h. The reaction mixture was allowed to warm to 25 °C, stirred for 8 h, and finally heated at 35–40 °C for 0.5 h. The resultant black mixture was poured into 1000 mL of cold H_2O. The aqueous mixture was acidified with 12 N HCl, then rendered basic with $NaHCO_3$ to pH 8, and extracted with three 500-mL portions of CH_2Cl_2. The CH_2Cl_2 extract was concentrated and the residual oil repeatedly diluted with EtOAc and concentrated until a semisolid material remained. This was triturated with two 50-mL portions of EtOAc and finally was dissolved in 50 mL of Me_2SO and 50 mL of H_2O on a steam bath, allowed to cool, and filtered to give 9.9 g (62%) of **8a**: mp 219–221 °C; IR (Nujol) 3125, 1630, 1590 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.78 (s, 3 H, N_1CH_3), 3.37 (s, 3 H, N_3CH_3), 5.83 (s, 1 H, C_4H), 6.60–7.30 (m, 6 H, ArH), 7.55 (q, 1 H, C_7H), 11.83 (br s, 1 H, OH); UV (CH_3OH) 263 nm (log ϵ 3.78), 285 (3.90); mass spectrum, *m/e* 269 (M^+·, 32%), 176 (M^+· – C_6H_4OH, 100%).

Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.51; H, 5.39; N, 15.26.

3,4-Dihydro-4-(2-hydroxyphenyl)-1,3,4-trimethylpyrido-[2,3-*d*]pyrimidin-2(1*H*)-one (8b). To a solution, under N_2, of 0.127 mol of LDA in 150 mL of dry THF, prepared as described above and held at –40 °C, was added a solution of 16.0 g (0.059 mol) of **4** in 150 mL of THF over 0.25 h. After the solution was warmed to 25 °C over 0.5 h, 3.9 mL (0.063 mol) of CH_3I was added, producing a temperature rise to 35 °C. After the solution was stirred for 2 h at ambient temperature, an additional 3.9 mL of CH_3I was added. The reaction mixture was allowed to stir for 6 h and then poured into 1000 mL of cold H_2O. The aqueous solution was acidified with 12 N HCl, rendered basic with $NaHCO_3$, and extracted with three 500 mL-portions of $CHCl_3$. The $CHCl_3$ solution was concentrated and the residual oil repeatedly treated with EtOAc and concentrated until a semisolid residue remained. This was triturated with two 50-mL portions of EtOAc and recrystallized from 50 mL of Me_2SO and 50 mL of H_2O at 100 °C to give 7.3 g (44%) of **8b**: mp 250–252 °C; IR (Nujol) 3115, 1618, 1595, 1585 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.84 (s, 3 H, C_4CH_3), 2.55 (s, 3 H, N_1CH_3), 3.38 (s, 3 H, N_3CH_3), 6.55–7.30 (m, 6 H, ArH), 7.44 (q, 1 H, C_7H), 11.43 (s, 1 H, OH); UV (CH_3OH) 240 nm (log ϵ 4.21), 271 (3.96), 283 (3.90), 324 (3.85); mass spectrum, *m/e* 283 (M^+·, 12.5%), 268 (M^+· – CH_3, 100%), 190 (M^+· – C_6H_4OH, 55.6%).

Anal. Calcd for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 68.05; H, 5.88; N, 14.49.

Deuteration Experiments. General Procedure. See Table I for results. To LDA (1, 2, or 3 molar equiv) in THF under N_2 at –40, 0, or 25 °C was added 0.50 g (0.00187 mol) of **4**. After the solution was stirred for the period of time noted, D_2O was added and the reaction mixture was poured into 100 mL of 5% aqueous NH_4Cl. The product was extracted into $CHCl_3$ and the chloroform was evaporated to give 0.45–0.48 g of crude product. This was recrystallized from 2.5 mL of EtOAc to give pure material which was analyzed for percent deuterium incorporation by mass spectral analysis.

Acknowledgment. We thank the staff of the Department of Physical and Analytical Chemistry, Schering-Plough Corporation, for microanalytical and spectral data. In particular we wish to thank Mr. Peter Bartner for his assistance in mass spectral interpretation.

Registry No. **3**, 6722-09-4; **4**, 73018-17-4; **8a**, 73018-18-5; **8b**, 73018-19-6; 1,3-dimethylurea, 96-31-1.

Useful Route to 1,6-Dioxaspiro[4.4]nonane and 1,6-Dioxaspiro[4.5]decane Derivatives[1]

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A wide variety of derivatives of 1,6-dioxaspiro[4.4]nonane and 1,6-dioxaspiro[4.5]decane, including certain insect pheromones, can be conveniently prepared by reaction of the lithium salts of protected alkynols with equimolar amounts of lactones followed by hydrogenation and acid-catalyzed deprotection and cyclization. Alkynols are satisfactorily protected either as their tetrahydropyranyl or as their 1-ethoxyethyl ethers; intermediates need not be isolated. Yields are variable, but products are readily obtainable in high purity regardless of yield.

Steroidal sapogenins[3a,b] and other moderately complex compounds such as monensin[3c] containing the 1,6-dioxaspirononane structure have been known for many years, but the discovery of simple 1,6-dioxaspironone and -decane natural products has occurred only recently. Derivatives of this class of compounds have been found in several plant species, of which chrysanthemum and hops are two examples.[3d] The discovery that this class of compounds includes insect pheromones is also a recent development, although various other acetal and ketal structures are well-known beetle pheromone components.[4] W. Francke and his collaborators have established the presence of 2-ethyl-1,6-dioxaspiro[4.4]nonane (**5**, **6**) in the aggregation pher-

(1) Approved as TA 15435 by the director of the Texas Agricultural Experiment Station in cooperation with ARS-USDA. Supported by the Texas Department of Agriculture Interagency Agreement IAC-0487 (78–79).

(2) (a) Oberlin College. (b) Texas A&M University.

(3) (a) Charles W. Shoppe, "Chemistry of the Steroids", Butterworth, London, 1964, pp 398–432; (b) "Natural Products Chemistry", Vol. 1, K. Nakanishi, Ed., Academic Press, New York, 1974, pp 476–84; (c) D. Perlman, "Fermentation Advances", Academic Press, New York, 1969, pp 517–40; (d) W. Francke and W. Reith, *Justus Liebigs Ann. Chem.*, 1 (1979), and references cited therein.

(4) (a) J. G. MacConnell, J. H. Borden, R. M. Silverstein, and E. Stokkink, *J. Chem. Ecol.*, **3**, 549 (1977); (b) G. T. Pearce, W. E Gore, and R. M. Silverstein, *J. Org. Chem.*, **41**, 2797 (1976); (c) R. M. Silverstein, R. G. Brownlee, T. E. Bellas, D. L. Wood, and L. E. Brown, *Science*, **159**, 889 (1968); (d) G. W. Kinzer, A. F. Fentiman, Jr., T. F. Page, Jr., R. L. Foltz, J. P. Vité, and G. B. Pitman, *Nature (London)*, **221**, 447 (1969); (e) V. Heeman and W. Francke, *Naturwissenschaften*, **63**, 344 (1976).

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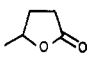
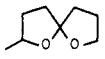
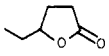
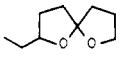
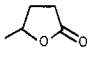
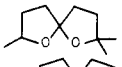
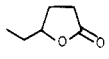
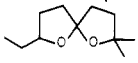
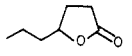
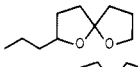
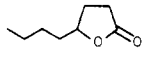
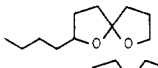
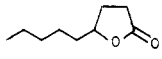
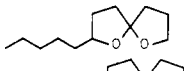
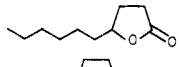
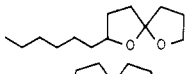
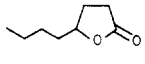
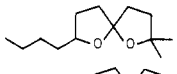
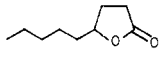
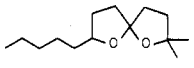
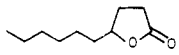
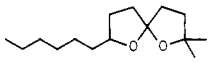
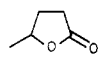
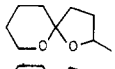
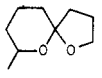
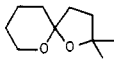
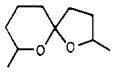
Table I. Summary of Synthetic Results

starting lactone	starting alkynol[a]	scale, mmol	method[b]	yield, %[c]	bp, °C	product[d]	no.[e]
	PR	55	C	25	flash distillation, 0.1 torr		2, 3
	PR	25	A	37	190-195, 1 atm		5, 6
	MB	50	A	49	170-180, 1 atm		7, 8
	MB	25	A	86	170-185, 1 atm		9, 10
	PR	35	C	30	flash distillation, 0.1 torr		13, 14
	PR	50	C	48	100-120, 25 torr		15, 16
	PR	55	C	49	65-72, 1 torr		17, 18
	PR	25	A	77	61-70, 0.1 torr		19, 20
	MB	56	B	32	50-52, 0.1 torr		23, 24
	MB	50	B	64	70-72, 0.1 torr		25, 26
	MB	56	B	65	75-80, 0.1 torr		27, 28
	PR	100	C	7.5	65-71, 27 torr		29
	B	37	A	21[f]			30, 31
	P	50	A	22	170-175, 1 atm		32
	MB	50	A	16	175-179, 1 atm		33
	P	50	A	36	173-175, 1 atm		34, 35

[a] Abbreviations: PR = propargyl alcohol, MB = 2-methyl-3-butyn-2-ol, B = 3-butyn-1-ol, and P = 4-pentyn-2-ol. [b] Methods (cf. Experimental Section): A involved use of the THP ether of the alkynol; B involved use of the (1-ethoxyethyl) ether of the alkynol; C involved in situ generation of the alkynol's 1-ethoxyethyl ether prior to methyllithium addition. [c] Yields refer to pure distilled material unless otherwise noted. [d] Routine characterization of products included IR, ^{1}H NMR, ^{13}C NMR, and mass spectra. For most compounds not previously reported, elemental analyses were also obtained and results have been provided to the Editor of this journal. [e] Compounds for which epimeric mixtures were obtained have been assigned two numbers. [f] Yield by GC.

omone of the "Kupferstecher" beetle[5] and found 2-methyl- and 7-methyl-1,6-dioxaspiro[4.5]decane (**30–32**) in the "antiaggression" scent of the wasp *Paravespula vulgaris*.[6]

Francke and Reith have described the synthesis of a variety of alkylated 1,6-dioxaspiro[4.4]nonanes from furan derivatives.[3d] An alternate route, suited to the preparation of symmetrically substituted structures, involves base-catalyzed dimerization of lactones followed by decarboxylation.[7] Such compounds have also been prepared from keto diacids[8a] and by lead tetraacetate treatment of α,ω-diols. Mori et al. have recently reported the synthesis of optically active chalcogran (**5, 6**), with alkylation of the dianion of α-acetyl-δ-butyrolactone by optically active epoxybutane as the key step.[9a,b] In this paper we present a preparative approach which complements these methods, is experimentally straightforward, and provides access to numerous 1,6-dioxaspiro[4.4]nonanes and 1,6-dioxaspiro[4.5]decanes from commercially available starting materials.

We previously reported[10] a synthesis of optically active 2-ethyl-1,6-dioxaspiro[4.4]nonane (**5, 6**) from an enantiomer of γ-caprolactone. In this preparation, the tetrahydropyranyl (THP) ether of propargyl alcohol was treated with 1 equiv of methyllithium, and the resulting alkynyllithium species was added to a solution of γ-caprolactone. A simple workup of the adduct was followed by hydrogenation, acid treatment, and distillation to give the desired dioxa spiro compound. Since numerous lactones are readily available and suitable alkynols may be pur-

(5) W. Francke, V. Heeman, B. Gerken, J. A. A. Renwick, and J. P. Vité, *Naturwissenschaften*, **64**, 590 (1977).
(6) W. Francke, G. Hindorf, and W. Reith, *Angew, Chem., Int. Ed. Engl.* **17**, 862 (1978).
(7) (a) V. Dedek and P. Trska, *Collect. Czech. Chem. Commun.*, **35**, 651 (1970); (b) F. Fittig, *Justus Liebigs Ann. Chem.*, **256**, 50 (1890); (c) K. T. Ström, *J. Prakt. Chem.*, **48**, 209 (1893).
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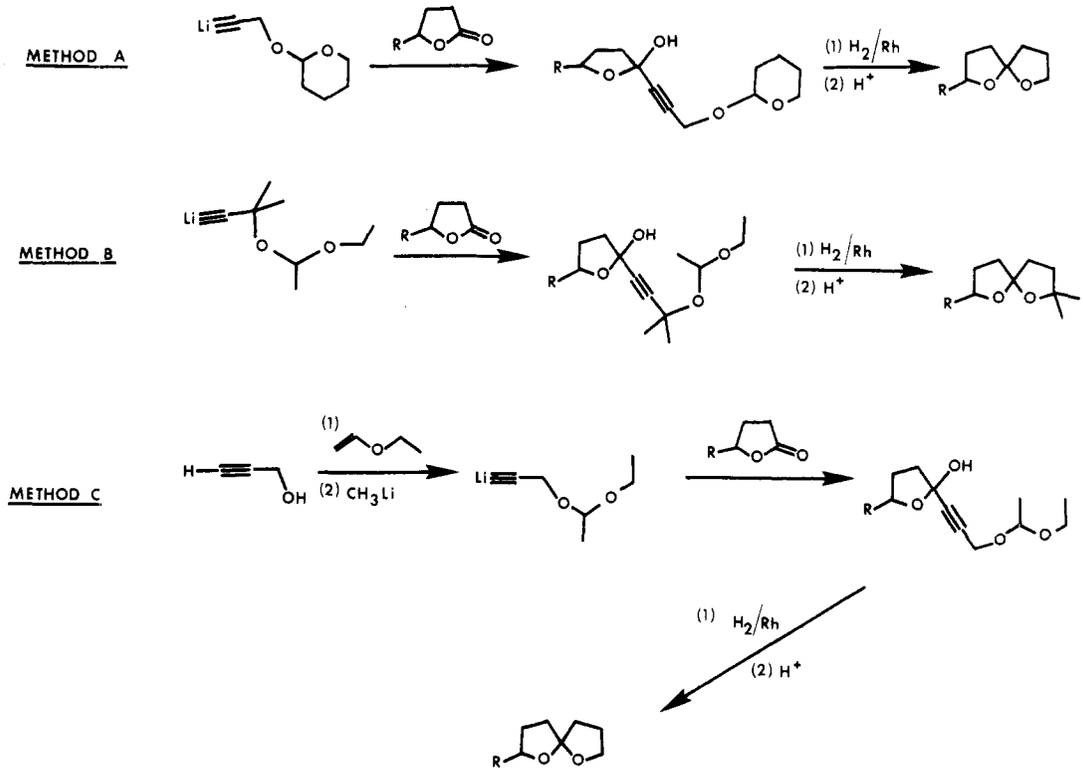
(9) (a) K. Mori, M. Sasaki, S. Tamada, T. Suguro, and S. Musada, *Heterocycles*, **10**, 111 (1978); (b) K. Mori, M. Sasaki, T. Suguro, and S. Musada, *Tetrahedron*, **35**, 1601 (1979).
(10) L. R. Smith, H. J. Williams, and R. M. Silverstein, *Tetrahedron Lett.*, 3231 (1978). An assignment of diastereomeric configurations was also made.

Scheme I. Summary of Synthetic Procedures



chased or prepared simply by the reaction of lithium acetylide with aldehydes, ketones, and epoxides, this approach appeared promising as a route to pheromone analogues and related compounds as well. Thus we prepared the series of 1,6-dioxaspiro[4.4]nonanes and 1,6-dioxaspiro[4.5]decanes appearing as products in Table I.

Our initial studies compared platinum oxide, palladium on charcoal, and rhodium on alumina as hydrogenation catalysts. The rhodium catalyst at 1 atm consistently gave comparable yields to the other catalysts and a noticeably cleaner reaction product (by GC analysis).[11] We accordingly used the rhodium catalyst in all subsequent preparations.

The THP protecting group used in early work reacted with the methanol hydrogenation solvent to produce methanol–THP ether as a byproduct, which made fractional distillation of the final product necessary. We subsequently tried ethyl vinyl ether[12] (procedure B; Scheme I) as an alternative protecting reagent for the starting alkynols. The 1-ethoxyethyl ether of 2-methyl-3-butyn-2-ol worked satisfactorily in the alkynylation sequence. However, attempts to prepare the 1-ethoxyethyl ether of propargyl alcohol gave very low distilled yields and masses of intractable black polymer. An alternative technique used the 1-ethoxyethyl ether of propargyl alcohol prepared in situ followed by carbanion formation using methyllithium and subsequent reaction with lactone (procedure C). This procedure was usually carried out by acid-catalyzed addition of propargyl alcohol to a slight excess of ethyl vinyl ether in diethyl ether, but ethyl vinyl ether can also be used successfully as the solvent for this step.

Yields, as seen in Table I, vary substantially. Some of the variation in yields is probably due to differences in procedures and workups used, but we have consistently obtained higher yields with substituted rather than the parent lactones. Addition of a lithium reagent to γ-butyrolactone and particularly to δ-valerolactone results in oily or gummy precipitates, a situation not found with the substituted lactones. We presume that these precipitates represent material lost to side reactions, but we have not made any attempt to characterize them in detail. In other reactions studied, the byproducts are probably water soluble and are efficiently removed by the aqueous washes within the sequence. Traces of unreacted starting lactone are easily removed by treatment with aqueous base prior to distillation. The purified products are colorless mobile liquids; the more volatile of these have a pronounced "minty" odor.

IR and NMR spectroscopic properties of our compounds will be summarized briefly. The IR spectra of the various 2-alkyl-1,6-dioxaspiro[4.4]nonanes are strikingly similar to each other. While prominent functional group bands do not appear, the strongest "fingerprint" band for all compounds in this series appears between 1000 and 1030 cm^{-1}. The 2-alkyl-7,7-dimethyl-1,6-dioxaspiro[4.4]nonanes show two or three relatively prominent bands in the range of 980–1080 cm^{-1}, as well as a characteristic, if somewhat weaker, absorption at about 860 cm^{-1}. The 860-cm^{-1} absorption also appears in the 2-substituted series, but less strongly. Derivatives of 1,6-dioxaspiro[4.5]decane have a multitude of narrow absorption bands in the fingerprint region, with the two or three most intense absorptions found between 1000 and 1100 cm^{-1}.

^1H NMR spectra of all the dioxa spirocycles show features characteristic of the ketal structure. Protons α to oxygen generally appear as multiplets in the region of δ 3.5–4.2. Ring and side-chain protons appear between δ 0.9 and 2.2. The observed complex multiplets have not lent

(11) For most of our work, we used a 5% Rh on alumina catalyst purchased from MCB. However, we have found the 0.5% Rh on alumina catalyst from Aldrich to be acceptable also, if the pellets are ground before use. Rh on alumina has been recommended as the catalyst of choice where hydrogenolysis must be avoided; see L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, 1967, p 979.

(12) (a) W. Reppe and Coworkers, *Justus Liebigs Ann. Chem.*, 601, 81 (1956); (b) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, p 387.

themselves to detailed interpretation. Much cleaner structural information is, however, available from ^{13}C NMR spectra (Table IIa,b, Supplementary Material). Shifts for carbon connected to oxygen have great diagnostic value. In the [4.4] series, C_5 appears at δ 114.56 when rings are unsubstituted, a value which increases only slightly with increasing substitution at C_2 and C_7. C_2 if unsubstituted appears at δ 66.78, if methyl substituted at $\delta \sim 76$ and if *n*-alkyl or dimethyl substituted at $\delta \sim 81$. Substitutents on one ring have little effect on shifts of carbons on the second ring. In the [4.5] systems, C_5 appears at δ 105.46 in the unsubstituted model and is shifted to δ 106.20 in the 2-dimethyl compound. C_2 appears at δ 66.89 when unsubstituted and δ 82.0 when dimethylated. C_7 appears at δ 61.37 when unsubstituted and at $\delta \sim 66$ with a single methyl. Peak assignments in the δ 29–31 area are somewhat arbitrary in the highly substituted compounds because of the large number of peaks appearing in this area. Studies of other compounds of this type will be made shortly.

Mass spectra of these compounds uniformly show loss of alkyl groups α to oxygen, as one would expect; more complex processes figure prominently as well. Losses of portions of one or the other ring to give "lactonic" fragments are generally found. Simple alkyl loss appears relatively more important in the [4.4] series than in the [4.5] series. Francke and Reith[3d] have presented a fragmentation scheme for the interpretation of mass spectra of various 1,6-dioxaspiro[4.4]nonane derivatives; one can, to some extent, similarly rationalize spectra of the 1,6-dioxaspiro[4.5]decanes. We have included some previously unavailable mass spectral fragmentation data in Table III (see Supplementary Material).

Experimental Section

Lactones were obtained commercially and used as received. Propargyl alcohol and 2-methyl-3-butyn-2-ol were distilled before use. THP ethers were prepared by standard methods.[13] Ethyl vinyl ether was dried by distillation from calcium hydride before use. Proton NMR spectra were run in chloroform-*d* with added Me_4Si by using a Perkin-Elmer Model R12B spectrometer. Carbon NMR spectra were run in benzene-d_6 by using a JEOL 90Q FT spectrometer. Data collection over 200 ppm used 16 384 memory units, giving 8192 real data points or a machine-limited accuracy of 0.025 ppm. Shift values are accurate to ±0.013 ppm. IR spectra were run on a Perkin-Elmer 727 instrument, and mass spectra were obtained on a Hitachi Perkin-Elmer RMS-4 instrument. Spectral characteristics of the dioxa spiro compounds are described and summarized in the discussion. Analytical and preparative GC were carried out by using a 2.4 m × 0.32 cm 6% OV-101 column, a 6 ft × 0.32 cm o.d. 6% SE-30 column, or a 1.8 m × 0.64 cm o.d. 8% Carbowax 20M column in a Carle Model 111 or a Perkin-Elmer Model 881 gas chromatograph. Microanalysis was done by Atlantic Microlab, Inc.

2-Ethyl-7,7-dimethyl-1,6-dioxaspiro[4.4]nonane (Procedure A). Anhydrous ether (50 mL) and 4.42 mL (25 mmol) of 2-methyl-3-butyn-2-ol THP ether were injected into a nitrogen-filled flask fitted with a septum, a magnetic stirring bar, and a nitrogen inlet. Methyllithium in ether (17.3 mL of a 1.45 M solution, 25 mmol) was added dropwise (rapidly), with stirring and cooling (ice bath). After ca. 5 min, the solution was transferred (transfer needle) (5 min) under slight nitrogen pressure into a second nitrogen-filled flask containing a magnetically stirred solution of 3.0 mL (26 mmol) of γ-caprolactone in 50 mL of anhydrous ether. The resulting solution was stirred for 3 h, 20 mL of 20% aqueous ammonium chloride was injected, and stirring was continued until all the precipitate dissolved. The organic layer was separated, washed with one portion of 1 M aqueous sodium bicarbonate, dried over anhydrous potassium carbonate, and evaporated to an oil. The oil was dissolved in 100 mL of anhydrous methanol and hydrogenated over 0.5 g of 5% Rh/alumina at 1-atm pressure. When hydrogen uptake ceased, the mixture was filtered (Celite) and most of the methanol was removed at reduced pressure. Concentrated hydrochloric acid (2 mL) was added and the solution was left at room temperature overnight. Water (30 mL) was added and the mixture was extracted with three 15-mL portions of hexane. Distillation gave 3.95 g (86%) of 2-ethyl-7,7-dimethyl-1,6-dioxaspiro[4.4]nonane as a mixture of epimers, bp 170–185 °C.

2-*n*-Pentyl-7,7-dimethyl-1,6-dioxaspiro[4.4]nonane (Procedure B). A 250-mL 3-necked round-bottom flask equipped with two septums and a nitrogen inlet was charged with 100 mL of anhydrous ether and 7.8 g (50 mmol) of 2-methyl-3-butyn-2-ol 1-ethoxyethyl ether. The flask was cooled in ice, and 36 mL (50 mmol) of 1.4 M methyllithium in ether was injected (2 min). After being stirred for 10 min, the solution was added (transfer needle) to a nitrogen-filled 500-mL flask (septum and magnetic stirring) charged with 100 mL of anhydrous ether and 7.8 g (50 mmol) of γ-nonalactone (10 min). The solution was stirred for 2 h at room temperature and quenched with 80 mL of ca. 6 M ammonium chloride/aqueous ammonia (equimolar) buffer. After all precipitate dissolved (4-min stirring), the phases were separated and the aqueous phase was extracted with two 30-mL portions of ether. The combined organic phases were dried over anhydrous potassium carbonate and evaporated at reduced pressure to an oil. The oil was dissolved in 100 mL of methanol and hydrogenated at 1 atm with 0.4 g of 5% Rh/alumina; after 3.5 h uptake ceased rapidly (90% of the theoretical uptake). The solution was filtered (Celite) and acidified with hydrochloric acid. After the solution was allowed to stand for 12 h at room temperature, the methanol was removed at reduced pressure, and the resulting oil was taken up in ca. 50 mL of pentane. The pentane solution was stirred over ca. 20 mL of 10% aqueous sodium hydroxide for 35 min, separated, and dried (potassium hydroxide). The solvent was removed by distillation at 1 atm, and the product was vacuum distilled to give 7.2 g (64%) of 2-*n*-pentyl-7,7-dimethyl-1,6-dioxaspiro[4.4]nonane, bp mostly 70–72 °C (0.1 torr).

2-*n*-Pentyl-1,6-dioxaspiro[4.4]nonane (Procedure C). A 250-mL 3-necked round-bottom flask was flushed with nitrogen and fitted with two septums, a nitrogen inlet, and a magnetic stirring bar. The flask was charged with 3.2 mL (55 mmol) of propargyl alcohol and 1 mmol of concentrated sulfuric acid. An ice bath was placed around the flask, and 5.7 mL (58 mmol) of ethyl vinyl ether was injected with stirring (1 min). After being stirred for 30 min, the mixture was diluted with 50 mL of anhydrous ether, and 39 mL (55 mmol) of 1.4 M methyllithium in ether was injected over several minutes. After being stirred 10 min, this solution was added (10 min) (transfer needle) to a rapidly stirred solution of 8.6 g (55 mmol) of γ-nonalactone in 100 mL of anhydrous ether in a 500-mL nitrogen-filled flask. The resulting solution was stirred at room temperature for 2 h and quenched with 50 mL of ammonium chloride/aqueous ammonia (cf. procedure B) buffer. After the solution was stirred for 5 min, the phases were separated and the aqueous phase was extracted with 30 mL of ether. The combined ethereal phases were dried over anhydrous potassium carbonate. The ether was removed at reduced pressure and the resulting orange oil was taken up in 100 mL of anhydrous methanol and hdyrogenated at 1 atm over 0.3 g of 5% Rh/alumina, consuming 70% of the theoretical in 130 min, at which time the reaction almost stopped. The solution was filtered (Celite) and acidified with 4 mL of 6 M aqueous hydrochloric acid. After 3 h, the methanol was removed on the rotary evaporator and the resulting oil was taken up in 50 mL of pentane. The pentane solution was stirred for 16 h over 50 mL of 20% aqueous sodium hydroxide solution; the layers were separated and the pentane layer was dried over potassium hydroxide. After removal of solvent by distillation at 1 atm, the residue was distilled at 1–2 torr (bp 65–74 °C, mostly boiling at 72 °C) to give 5.3 g (49%) of 2-*n*-pentyl-1,6-dioxaspiro[4.4]nonane.

2-Methyl-3-butyn-2-ol 1-Ethoxyethyl Ether. A 250-mL round bottom flask containing a magnetic stirring bar was charged with 58 mL (0.59 mol) of 2-methyl-3-butyn-2-ol and 1 drop of concentrated sulfuric acid. The flask was fitted with a 100-mL pressure-equalizing addition funnel and cooled in an ice bath. Freshly distilled ethyl vinyl ether (90 mL, 0.94 mol) was added (15 min) with stirring; the reaction temperature remained under

(13) D. N. Robertson, *J. Org. Chem.*, **25**, 931 (1960).

10 °C during the addition. After 15 min more, ca. 2 g of potassium carbonate was added and stirring was continued for another 10 min. The product was distilled at 1 atm to give 71 g (77%) of the desired 1-ethoxyethyl ether, bp mostly 146 °C. NMR and IR spectra were satisfactory.

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Registry No. *cis*-**2**/**3**, 73137-44-7; *trans*-**2**/**3**, 73137-45-8; *cis*-**5**/**6**, 73208-56-7; *trans*-**5**/**6**, 73208-57-8; *cis*-**7**/**8**, 73137-46-9; *trans*-**7**/**8**, 73137-47-0; *cis*-**9**/**10**, 73137-48-1; *trans*-**9**/**10**, 73137-49-2; *cis*-**13**/**14**, 73137-50-5; *trans*-**13**/**14**, 73137-51-6; *cis*-**15**/**16**, 73137-52-7; *trans*-**15**/**16**, 73137-53-8; *cis*-**17**/**18**, 73137-54-9; *trans*-**17**/**18**, 73137-55-0; *cis*-**19**/**20**, 73137-56-1; *trans*-**19**/**20**, 73137-57-2; *cis*-**23**/**24**, 73137-58-3; *trans*-**23**/**24**, 73137-59-4; *cis*-**25**/**26**, 73137-60-7; *trans*-**25**/**26**, 73137-61-8; *cis*-**27**/**28**, 73137-62-9; *trans*-**27**/**28**, 73137-63-0; **29**, 177-23-1; *cis*-**30**/**31**, 73137-64-1; *trans*-**30**/**31**, 73137-65-2; **32**, 73046-13-6; **33**, 73137-66-3; **34**, 73208-58-9; PR, 107-19-7; PR THP ether, 6089-04-9; PR 1-ethoxyethyl ether, 18669-04-0; MB, 115-19-5; MB THP ether, 27943-46-0; MB 1-ethoxyethyl ether, 39807-00-6; B, 927-74-2; B THP ether, 40365-61-5; P, 2117-11-5; P THP ether, 58654-09-4; dihydro-5-methyl-2(3*H*)-furanone, 108-29-2; 5-ethyldihydro-2(3*H*)-furanone, 695-06-7; dihydro-5-propyl-2(3*H*)-furanone, 105-21-5; 5-butyldihydro-2(3*H*)-furanone, 104-50-7; dihydro-5-pentyl-2(3*H*)-furanone, 104-61-0; 5-hexyldihydro-2(3*H*)-furanone, 706-14-9; tetrahydro-2*H*-pyran-2-one, 542-28-9; dihydro-2(3*H*)-furanone, 96-48-0; ethyl vinyl ether, 109-92-2.

Supplementary Material Available: ^{13}C NMR data for all compounds and mass spectral data for compounds not previously reported (4 pages). Ordering information is given on any current masthead page.

Alkyllithium Reagents from Alkyl Halides and Lithium Radical Anions[1]

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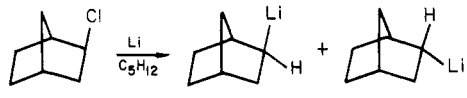
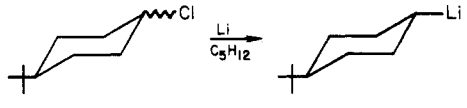
The reaction of alkyl halides with three different lithium radical anions, lithium naphthalene (LiN), lithium di-*tert*-butylnaphthalene (LiDBN), and lithium di-*tert*-butylbiphenyl (LiDBB), was studied. The reaction of alkyl halides with an excess of LiN, LiDBN, or LiDBB in THF at −78 °C leads to a consistently high yield (96–100%) of reduction products (RH, RLi) with a high degree of formation of RLi (anion trapping 93–95%) in the case of LiDBB. LiDBN consistently produces high yields of reduction products (89–99%) with widely variable amounts of anion trapping (21–88%), while LiN provides variable yields of reduction (39–99%) and anion trapping (24–65%). Variation of the concentration of lithium bromide and naphthalene and the ratio of alkyl halide to naphthalene in conjunction with the use of deuterium tracer experiments provided evidence consistent with a competition between metalation of the lithium dihydronaphthalenedicarboxylate by alkyllithium and carbonation of alkyllithium in the carbonation step of the analysis.

Alkyllithium reagents are potentially very valuable synthetic reagents for organic synthesis. Often the yields of products from addition reactions with ketones and nitriles exceed those of the more common Grignard reagents,[2] while synthetic sequences which start with the formation of lithium dialkylcuprates from cuprous halide employ lithium reagents, since the Grignard alternative generally cannot be substituted.[3] However, lithium reagents, other than those commercially available, have not achieved as widespread use as one might expect in view of their superior properties. This can be ascribed to the fact that their preparation from the halide and lithium metal often gives rather low yields or requires considerable "magic" in order to attain high yields.[4,5] For example, Applequist and Chmurny have reported that treatment of *exo*-2-norbornyl chloride with lithium metal in refluxing pentane gives yields of the lithium reagent as high as 33% but averaging about 10%,[6] while Alexandrou was unsuccessful



(1)

4:1, 10% yield



(2)

35% yield

in a variety of attempts to prepare (4-*tert*-butylcyclohexyl)lithium from the bromide.[7] Glaze and Selman later prevailed in the preparation of (4-*tert*-butylcyclohexyl)-lithium utilizing the chloride with lithium containing 1% sodium.[8] This illustrates another difficulty of the conventional procedure—bromides give much poorer yields than chlorides. This is undoubtedly due to the greater tendency of bromides to undergo side reactions (coupling) with lithium reagents.

Clearly, the development of a reaction sequence which would overcome the deficiencies in the traditional preparation of alkyllithium reagents would be a significant step forward for synthetic and mechanistic investigations. With this background in mind, a study aimed at uncovering a

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